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Inhibition of Human Melanoma C8161 Colony Forming Ability  
by 12 Different Antisense ODNs

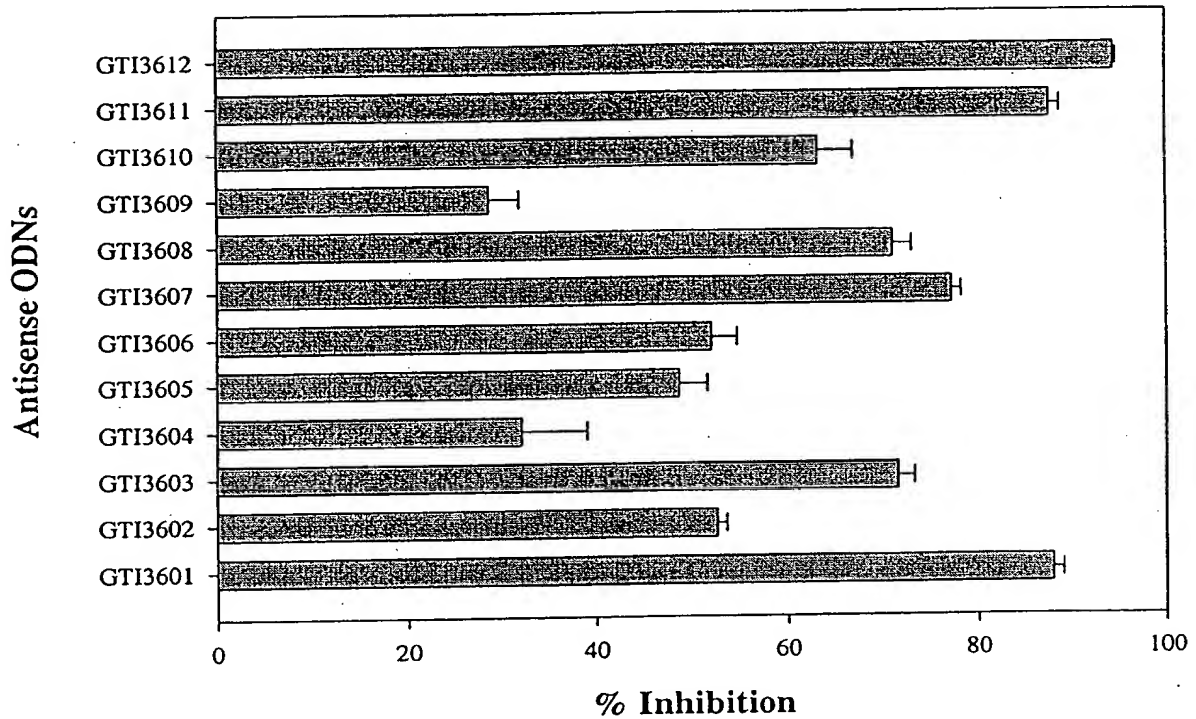


FIG. 1A



APPLICANT(S): Wright et al.  
TITLE: NEUROPILIN ANTISENSE OLIGONUCLEOTIDE  
SEQUENCES AND METHODS OF USING SAME TO  
MODULATE CELL GROWTH  
Application No.: 09/296,264 Filing Date: April 22, 1999  
Docket No.: MBM1250-2

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**Inhibition of Human Lung Cancer A549 Colony Forming Ability  
by 12 Different Antisense ODNs**

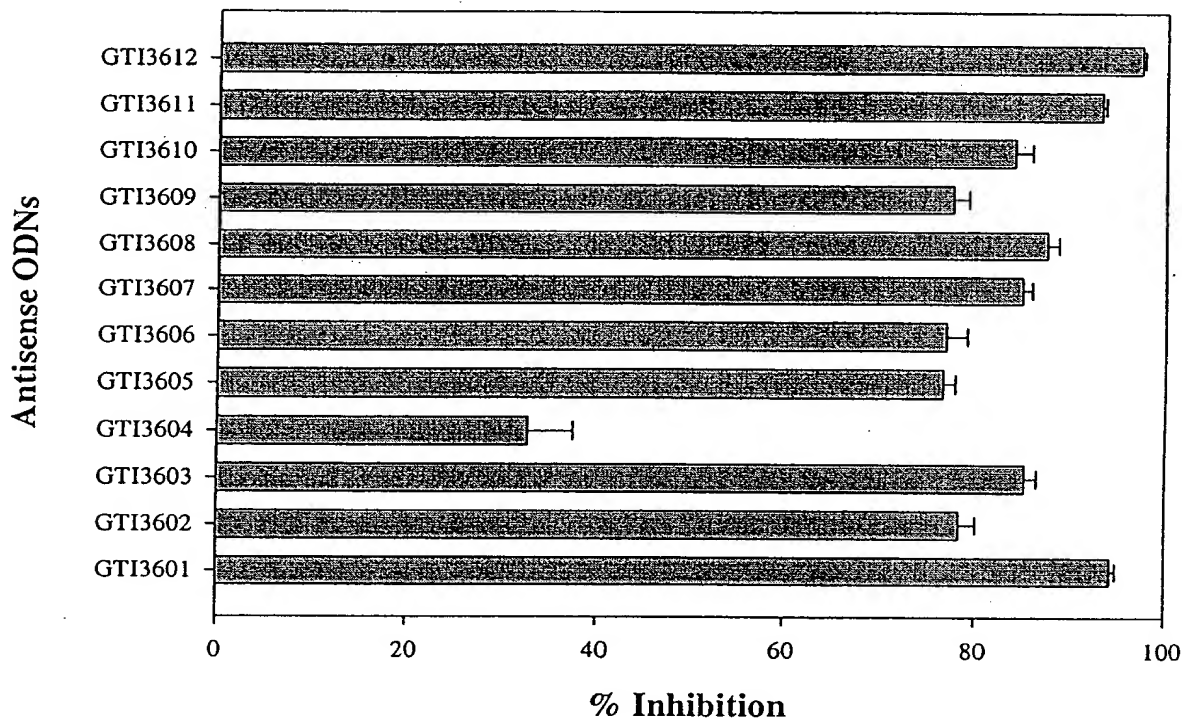


FIG. 1B



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Inhibition of Human melanoma A2058 Colony Forming Ability  
by 12 Different Antisense ODNs

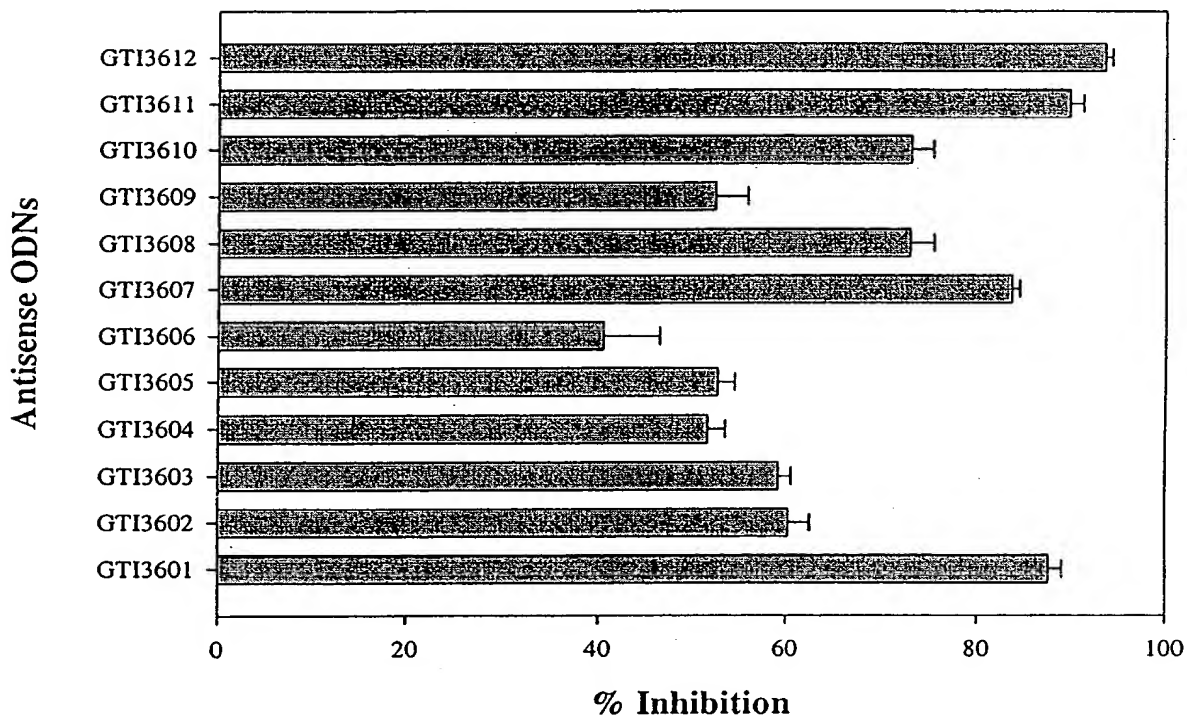


FIG. 1C



APPLICANT(S): Wright et al.  
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**Inhibition of Human Colon Cancer HT-29 Colony Forming Ability  
by 12 Different Antisense ODNs**

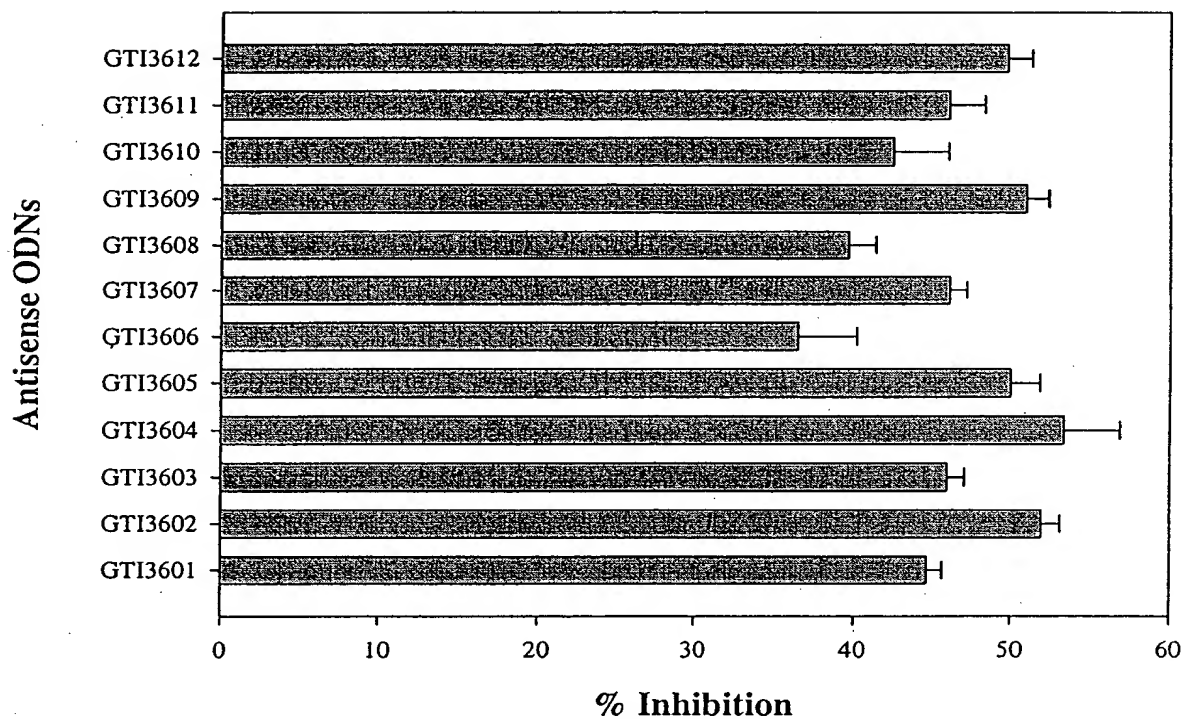


FIG. 1D



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**Inhibition of Human Prostate Cancer PC-3 Colony Forming Ability  
by 12 Different Antisense ODNs**

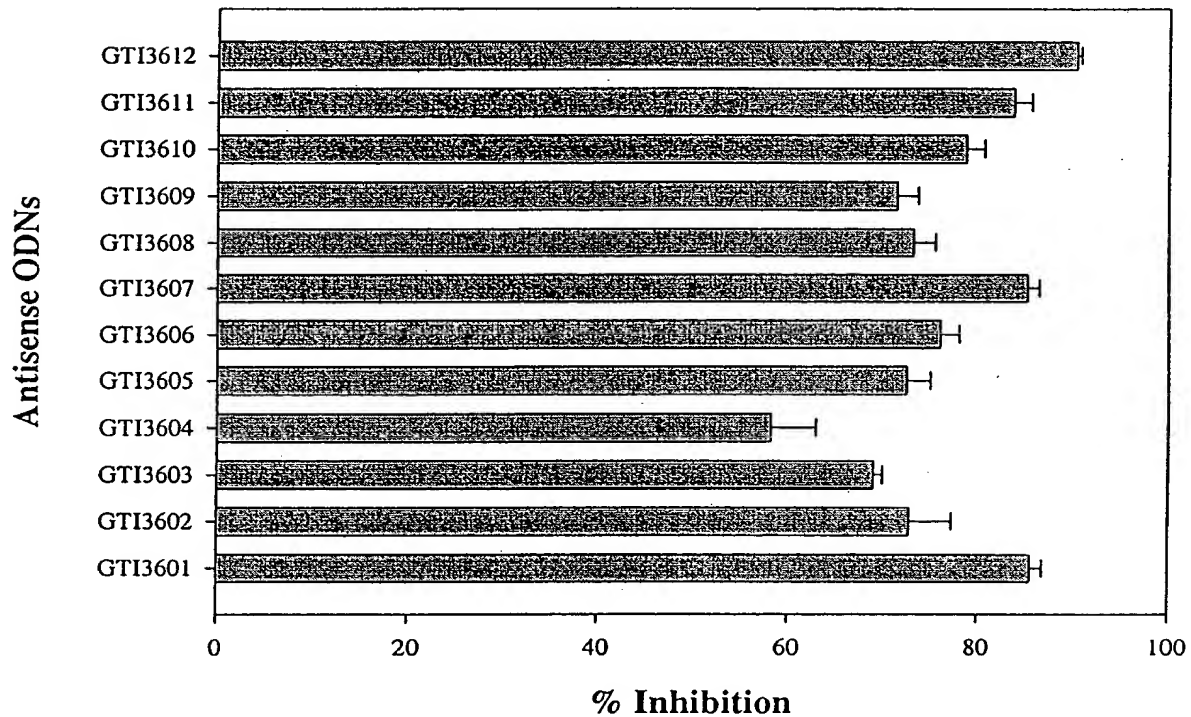


FIG. 1E



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**Inhibition of Human Pancreatic Cancer AsPC-1 Colony Forming Ability  
by 12 Different Antisense ODNs**

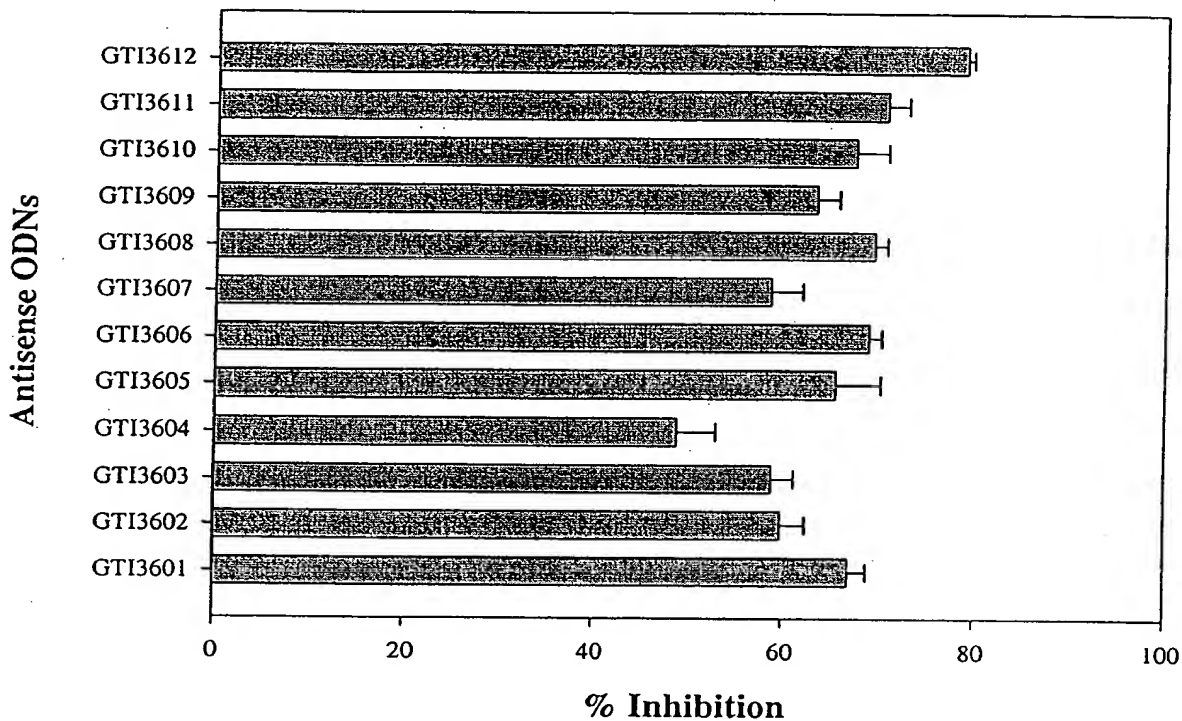


FIG. 1F



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## Examples of Decreased mRNA Levels following Treatment with Antisense ODNs

### Breast Cancer Cells (MDA-MB-231)

Control GTI3611 GTI3612 GTI3604 GTI3603 GTI3602 GTI3601



FIG. 2A

### Melanoma Cells (A2058)

Control GTI3601 GTI3610 GTI3611 GTI3612



FIG. 2B



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### Effects of GTI3602 Antisense ODN treatment on Human Tumor Growth in Mice

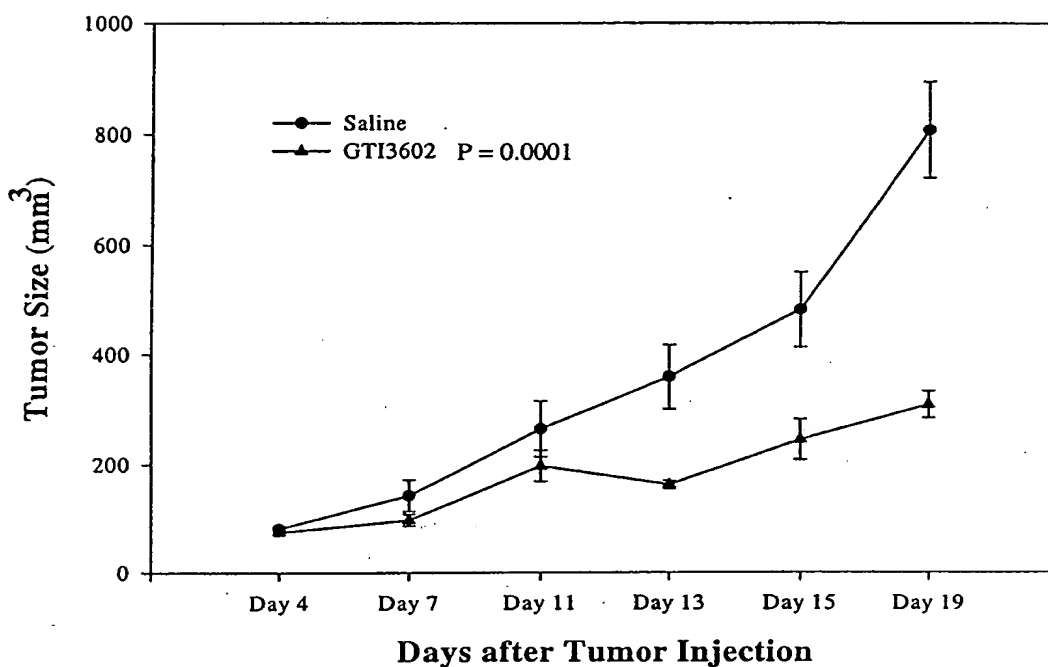


FIG. 3A

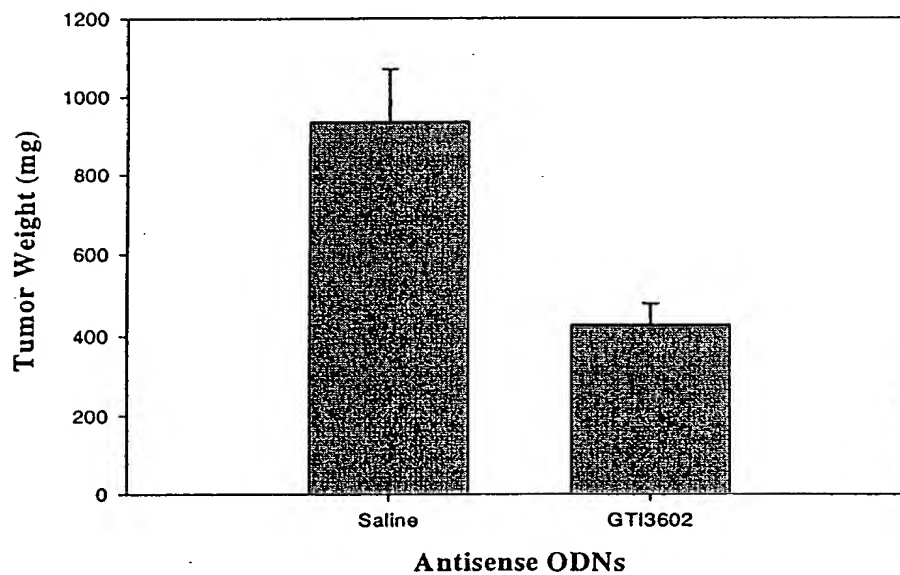


FIG. 3B





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## Reduction of Tumor Metastases

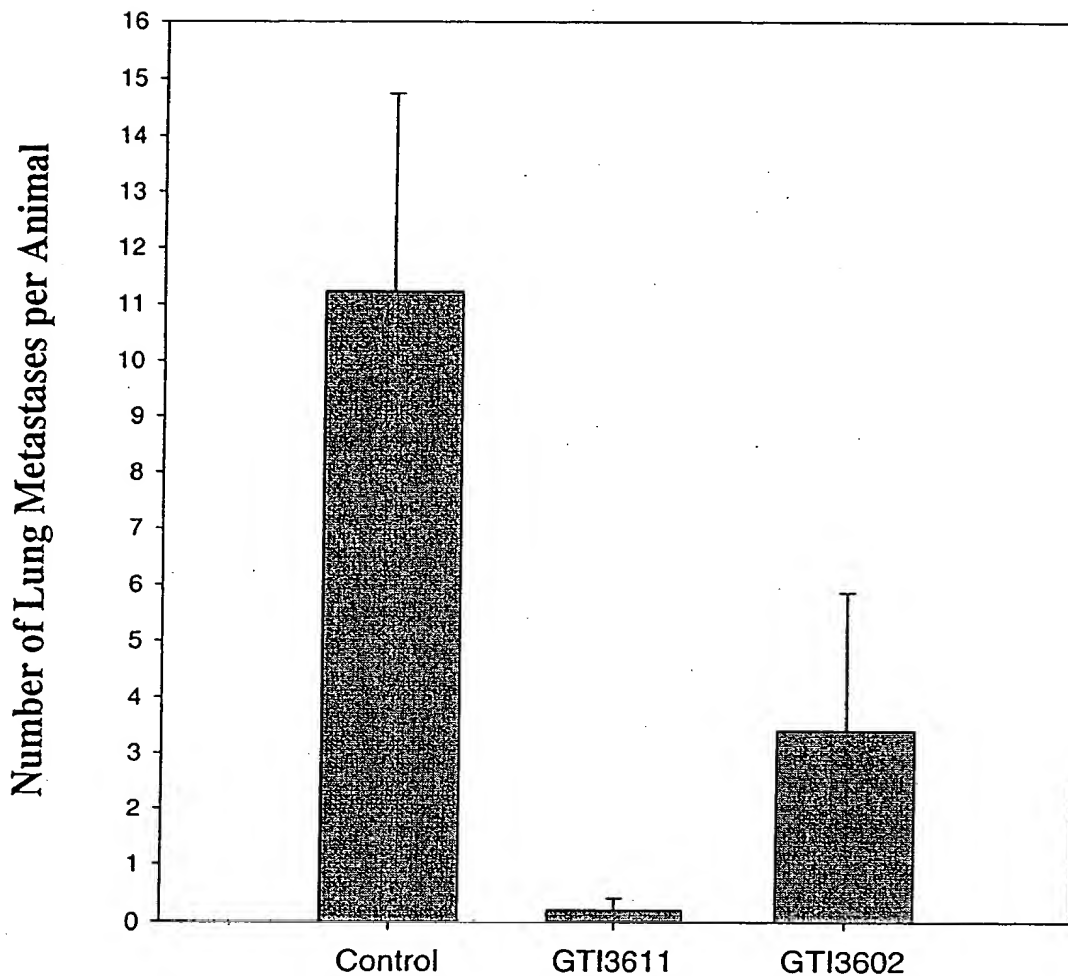


FIG. 4



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660  
720  
780  
840  
900  
960  
1020  
1080

ATGAGAGGG GGCTGCCGCT CCTCTGCGCC GTGCTCGCCC TCGTCTCTCGC CCGGCCGGGC  
GCTTTTCGCA ACGATGAATG TGGCGATACT ATAAAATTTG AAAGCCCGCG GTACCTTACA  
TCTCCTGGTT ATCCTCAATC TTATCACCCA AGTGAAAAAT GCGAATGGCT GATTCAGGCT  
CCGGACCCAT ACCAGAGAAT TATGATCAAC TTCAACCCCTC ACTTCGATTT GGAGGACAGA  
GACTGCAAGT ATGACTACGT GGAAGTCTTC GATGGAGAA ATGAAATGG ACATTTTAGG  
GGAAGTTCT GTGGAAGAT AGCCCTCCT CCTGTTGTTGTT CTTCAGGGCC ATTCTTTT  
ATCAAAATTTG TCTCTGACTA CGAAACACAT GGTGCAAGAT TTCCATACG TTATGAATTT  
TTCAAGAGAG GTCCTGAATG TTCCAGAAC TACACACAC CTAATGGAGT GATAAAGTCC  
CCCGGATTCC CTGAAAAATA TCCCAACAGC CTTGAATGCA CTTATATTGT CTTTGGGCCA  
AAGATGTCAG AGATTATCCT GGAATTTGAA AGCTTTGACC TGGAGCCTGA CTCAAATCCT  
CCAGGGGGA TGTTCGTCTG CTACGACCGG CTAGAAATCT GGGATGGATT CCCTGATGTT  
GGCCCTCACA TTGGGGGTTA CTGTGGACAG AAAACACCA GTCGAATCCG ATCCTCATCG  
GGCATTCTCT CCATGGTTT TACACCGAC AGCGGATAG CAAAGAAGG TTTCTCAGCA  
AACTACAGTG TCTTGCAGAG CAGTGTCTCA GAAGATTTC AATGTATGGA AGCTCTGGGC  
ATGGAATCAG GAGAAATTCA TTCTGACCAG ATCACAGCTT CTTCCAGTA TAGCACCAC  
TGGTCTGCAG AGCGTCCCG CCTGAACAC CCTGAGATG GGTGGACTCC CGGAGAGGAT  
TCCTACCGAG AGTGGATACA GGTAGACTTG GGCCTTCTGC GCTTGTCTC GGTGTCTGGG  
ACACAGGGCG CCATTTCAAA AGAAACCAAG AAGAATATT ATGTCAAGAC TTACAAGATC

FIG. 5-1



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1140 GACGTTAGCT CCAACGGGGA AGACTGGATC ACCATAAAG AAGGAACAA ACCTGTTCTC  
1200 TTTACGGGAA ACACCAACCC CACAGATGTT GTGGTTGCAG TATTCGCCAA ACCACTGATA  
1260 ACTCGATTG TCCGAATCAA GCCTGCAACT TGGGAAACTG GCATATCTAT GAGATTGAA  
1320 GTATACGGTT GCAAGATAAC AGATTATCCT TGCTCTGGA TGTGGGTAT GGTGCTGGA  
1380 CTTATTTCTG ACTCCAGAT CACATCATCC AACCAGGAG ACAGAAACTG GATGCCCTGAA  
1440 AACATCCGCC TGGTAACCAAG TCGCTCTGGC TGGCACTTC CACCCGCACC TCATTCCCTAC  
1500 ATCAATGAGT GGCTCCAAAT AGACCTGGG GAGGAGAAGA TCGTGAGGG CATCATCAT  
1560 CAGGTTGGGA AGCACCGAGA GAACAAAGTG TTCAATGAGGA AGTTCAAGAT CGGTACAGC  
1620 AACAAACGGCT CGGACTGGAA GATGATCATG GATGACAGCA AAGCAAGGC GAAGTCTTTT  
1680 GAGGGCAACA ACAACTATGA TACACCTGAG CTGCGGACTT TTCCAGCTCT CTCCACGCGA  
1740 TTCAATCAGGA TCTACCCCGA GAGAGCCACT CATGGCGGAC TGGGGCTCAG AATGGAGCTG  
1800 CTGGGCTGTG AAGTGAAGC CCTACAGCT GGACCGACCA CTCCCAACGG GAACCTTGGTG  
1860 GATGAATGTG ATGACGACCA GGCCAACTGC CACAGTGGAA CAGGTGATGA CTTCCAGCTC  
1920 ACAGGTGGCA CCACTGTGCT GGCCACAGAA AAGCCACGG TCATAGACAG CACCATACAA  
1980 TCAGAGTTTC CAACATATGG TTTTAACTGT GAATTTGGCT GGGGCTCTCA CAAGACCTTC  
2040 TGCCACTGGG AACATGACAA TCACGTGCGAG CTCAAGTGGG GTGTGTTGAC CAGCAAGACG  
2100 GGACCCATTC AGGATCACAC AGGAGATGGC AACTTCATCT ATTCCCAAGC TGACGAAAT  
2160 CAGAAGGGCA AAGTGGCTCG CCTGGTGAGC CCTGTGGTTT ATTCCAGAA CTCTGCCAC  
2220 TGCAATGACCT TCTGGTATCA CATGTCTGGG TCCACGTCG GCACACTCAG GGTCAAACTG  
2280 CGCTACCAGA AGCCAGAGGA GTACGATCAG CTGGTCTGGA TGGCCATTGG ACACCAAGGT  
2340 GACCACTGGA AGGAAGGGCG TGTCTTGCTC CACAAGTCTC TGAAACTTTA TCAGGTGATT  
2400 TTCGAGGGCG AATCGGAAA AGGAAACCTT GGTGGATTG CTGTGGATGA CATTAGTATT  
2460 AATAACCA CA TTTCACAAGA AGATTGTGCA AACCAGCAG ACCTGGATAA AAGAAACCCA  
2520 GAAATTAAA TTGATGAAAC AGGGAGCACG CCAGGATACG AAGTGAAGG AGAAGGTGAC  
2580 AAGAACATCT CCAGGAAGCC AGGCAATGTG TTGAAGACCT TAGAACCCAT CCTCATCACC  
2640 ATCATAGCCA TGAGCGCCCT GGGGTCTCTC CTGGGGCTG TCTGTGGGGT CGTGTGTAC  
2700 TGTGCCCTGT GGCATAATGG GATGTCAGAA AGAACTTGT CTGCCCTGGA GAACATAAAC  
2760 TTTGAACCTG TGGATGGTGT GAAATTGAAA AAGACAAAC TGAATACACA GAGTACTTAT  
2772 TCGGAGGCAT GA

FIG. 5-2



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60 ATGGAGAGGG GCGTGGCGTT GCTGTGGGCC ACGCTCGCCC TTGCCCTCGC CCTGGGGGCT  
120 TTCCGCAGCG ATAAATGTGG CGGGACTATA AAAATTGAAA ACCCGGGTA CCTTACATCT  
180 CCCGGCTACC CTCATTCTTA CCATCCAAGT GAGAAATGTG AATGGCTAAT CCAAGCTCCG  
240 GAGCCCTACC AGAGRATCAT GATCAACTTC AACCCACATT TCGATTGGA GGACAGAGAC  
300 TGCAAGTATG ACTATGTGA AGTGATCGAT GGAGAGATG AAGGTGGCCG CCTGTGGGGG  
360 AAGTTCTGTG GGAAGATCGC ACCTTCACCT GTGGTGTCTT CAGGGCCATT TCTCTTCATC  
420 AAATTTGTCT CTGACTATGA GACCCACGGG GCAGGATTTT CCATCCGCTA TGAATCTTTC  
480 AAGAGAGGGC CCGAATGTTT TCAGAACTAT ACAGCACCTA CTGGAGTGAT AAAGTCCCTT  
540 GGGTTCCCTG AAAAATACCC CAACAGCTTG GAGTGCACCT ACATCATCTT TGCACCAAAG  
600 ATGTCTGAGA TAATCCTAGA GTTTGAAAGT TTTGACCTGG AGCAAGACTC AAATCCTCCC  
660 GGAGGAATGT TCTGTGCGCTA TGACCGGCTG GAGATCTGGG ATGGATTCCC TGAAGTTGGC  
720 CCTCACATTG GCGTTACTG TGGGCAGAAA ACTCCTGGCC GGATCCGCTC CTCCTTCAGGC  
780 ATTCTATCCA TGGTCTTCTA CACTGACAGC GCAATAGCAA AGGAAGGTTT CTCAGCCAAC  
840 TACAGCGTGC TGCAGAGCAG CATCTCTGAA GATTTCAAGT GTATGGAGGC TCTGGGCATG  
900 GAATCTGGAG AGATCCATTG TGACCCAGATC ACTGCATCTT CCCAGTATGG TACCAACTGG  
960 TCTGTTGAGC GCTCCCGCCT GAACTACCTT GAAAACGGGT GGACACCCAGG AGAGGACTCC  
1020 TACAGGGAGT GGATCCAGGT GGACTTGGC CTCCTGCGAT TCGTTACTGC TGTGGGGACA  
1080 CAGGGTGCCA TTTCCAAAGG AACCAAGAAG AAATATTATG TCAAGACTTA CAGAGTAGAC  
1140 ATCAGCTCCA ACGGAGAGGA CTGGATCACC CTGAAGGAGG GAAATRAAGC CATTTATCTT  
1200 CAGGGAACA CCAATCCCAC GGATGTTGTC TTTGGAGTTT TCCCAAACC ACTGATAACT  
1260 CGATTTGTCC GAATCAAACC TGCATCCTGG GAAACTGGAA TATCTATGAG ATTTGAAAGT  
1320 TATGGCTGCA AGATAACAGA TTACCCCTGC TCTGGAATGT TGGGCATGGT GTCTGGACTT  
1380 ATTTCAGACT CCCAGATTAC AGCATCCAAC CAAGGAGACA GGAACCTGGT GCCAGAAAAC  
1440 ATCCGCCCTG TGACCCAGTCG AACCGGCTGG GCCCTGCCAC CCTCACCCCA CCCATACATC  
1500 AATGAATGGC TCCAAGTGA CCTGGGAGAT GAGAAGATAG TAAGAGGTGT CATCATTTCAA  
1560 GGTGGGAAGC ACCGAGAAAA CAAAGTGTTT ATGAGGAAGT TCAAGATCGC CTACAGTAAC  
1620 AATGGTTCTG ACTGGAAAAAT GATCATGGAT GACAGCAAGC GCAAGGCTAA GTCTTTTGAA  
1680 GGCAACAACA ACTATGACAC ACCTGAGCTC CGGGCCTTTA CACCTCTCTC CACAAGATTC

FIG. 6-1



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1740	ATCAGGATCT	ACCCCGAGAG	AGCCACACAT	AGTGGGCTCG	GACTGAGGAT	GGAGCTACTG
1800	GGCTGTGAAG	TAGAAGTGCC	TACAGCTGGA	CCCACGACAC	CCAATGGGAA	CCCCGTGGAC
1860	GAGTGTGACG	ATGACCAGGC	CAACTGCCAC	AGTGGCACAG	GTGATGACTT	CCAGCTCACA
1920	GGAGGCACCA	CTGTCTCTGGC	CACAGAGAAAG	CCCACCATTA	TAGACAGCAC	CATCCAATCA
1980	GAGTTCCCGA	CATACGGTTT	TAACTGCGAG	TTTGGCTGGG	GCTCTCACAA	GACATTCTGC
2040	CACTGGGAAC	ATGACAGCCA	CGCGCAGCTC	AGGTGGAGGG	TGCTGACCAG	CAAGACGGGG
2100	CCCATTGAGG	ACCACACAGG	AGATGGCAAC	TTCATCTATT	CCCAAGCTGA	TGAAAATCAG
2160	AAAGGCAAAG	TAGCCCGCCT	GGTGAGCCCT	GTGGTCTATT	CCGAGAGTTC	TGCCCACTGC
2220	ATGACCTTCT	GGTATCACAT	GTCCGGCTCT	CATGTGGGTA	CACTGAGGGT	CAAACTGCAC
2280	TACCAGAAGC	CAGAGGAATA	TGATCAACTG	GTCTGGATGG	TGGTCGGGCA	CCAAGGAGAC
2340	CACTGGAAGG	AAGGGCGTGT	CTTGCTGCAC	AAATCTCTGA	AACTGTATCA	GGTTATTTT
2400	GAAGGTGAAA	TCGGAAAAGG	AAACCTCGGT	GGGATTGCTG	TGGATGATAT	CAGTATTAAAC
2460	AACCACATTC	CTCAGGAGGA	CTGTGCAAAA	CCAACAGACC	TAGATAAAAA	GAACACAGAA
2520	ATTAAATAAG	ATGAAACAGG	GAGCACCCCA	GGATATGAAG	AAGGGAAGG	CGACAAGAAC
2580	ATCTCCAGGA	AGCCAGGCCAA	TGTGCTTAAG	ACCCTGGACC	CCATCCTGAT	CACCATCATA
2640	GCCATGAGTG	CCCTGGGGGT	GCTCCTGGGT	GCAGTCTGTG	GAGTTGTGCT	GTACTGTGCC
2700	TGTTGGCACA	ATGGGATGTC	GGAAAGGAAC	CTATCTGCCC	TGGAGAACTA	TAACTTTGAA
2760	CTTGTGGATG	GTGTAAAGTT	GAATAAAGAT	AACTGAACCC	CACACAGTAA	TTACTCAGAG
2766	GGGTGA					

FIG. 6-2



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TTTTTTTTT	TTTTTTTTT	TTTTTTTTT	TTTTTTTTT	TTTTTCTCC	TTCTTCTTCT	TCCTGAGACA	60
TGGCCCGGC	AGTGGCTCCT	GGAAGAGGAA	CAAGTGTGGG	AAAAGGGAGA	GGAATCGGA	120	
GCTAAATGAC	AGGATGCAGG	CGACTTGAGA	CACAAAAGA	GAAGCGCTTC	TGCGGAATTC	180	
AGGCATTGCC	TGCGCGCTAG	CCTTCCCCCG	CAAGACCCCG	TGAGGATTTT	ATGGTTCTTA	240	
GGCGGACTTA	AGAGCGTTTC	GGATTGTAA	GATTATCGTT	TGCTGGTTTT	TGCTCCGCGC	300	
AATCGTGTTC	TCCTGCGGCT	GCCTGGGGAC	TGGCTTGGCG	AAGGAGGATG	GAGAGGGGGC	360	
TGCCGTGCT	GTGCGCCACG	CTGCGCCCTG	CCCTCGCCCT	GGCGGGCGCT	TTCCGCGAGG	420	
ACAAATGTGG	CGGGACCATA	AAAATCGAAA	ACCCAGGGTA	CCTCACATCT	CCCGGTTACC	480	
CTCATTTCTTA	CCATCCCAAGT	GAGAAAGTGTG	AATGGCTAAT	CCAGCTCCG	GAACCCCTACC	540	
AGAGAAATCAT	AATCAACTTC	AACCCACATT	TCGATTTGGA	GGACAGAGAC	TGCAAGTATG	600	
ACTACGTGGA	AGTAATTGAT	GGGAGAAATG	AAGCGGGCCG	CCTGTGGGG	AAGTTCTGTG	660	
GGAGATTGC	ACCTTCTCCT	GTGGTGTCTT	CAGGGCCCTT	TCTCTTCATC	AAATTTGTCT	720	
CTGACTATGA	GACACATGGG	GCAGGGTTTT	CCATCCGCTA	TGAAATCTTC	AAGAGAGGGC	780	
CCGAATGTTT	TCAGAACTAT	ACAGCACCTA	CTGGAGTGAT	AAAGTCCCT	GGGTTCCTCTG	840	
AAAAATACCC	CAACTGCTTG	GAGTGACCT	ACATCATCTT	TGCACCAAG	ATGTCTGAGA	900	
TAATCCTGGA	GTTTGAAAGT	TTTGACCTGG	AGCAAGACTC	GAATCCTCCC	GGAGGAATGT	960	
TCTGTGCTA	TGACCGGCTG	GAGATCTGGG	ATGGATTCCC	TGAAGTTGGC	CCTCACATTG	1020	
GGCGTTATTG	TGGGCAGAAA	ACTCCTGGCC	GGATCCGCTC	CTCTTCAGGC	GTTCTATCCA	1080	
TGGTCTTTTA	CACTGACAGC	GCAATAGCAA	AAGAAGGTTT	CTCAGCCAAAC	TACAGTGTGC	1140	
TACAGAGCAG	CATCTCTGAA	GATTTTAAGT	GTATGGAGGC	TCTGGGCATG	GAATCTGGAG	1200	
AGATCCCATTC	TGATCAGATC	ACTGCATCTT	CACAGTATGG	TACCAACTGG	TCTGTAGAGC	1260	
GCTCCCGCCT	GAACTACCTT	GAAATGGGT	GGACTCCAGG	AGAAGACTCC	TACAAGGAGT	1320	
GGATCCAGGT	GGACTTGGGC	CTCCTGCGAT	TCGTTACTGC	TGTAGGGACA	CAGGGTGCCA	1380	
TTTCCAAAGGA	AACCAAGNAG	AAATATTATG	TCAAGACTTA	CAGAGTAGAC	ATCAGCTCCA	1440	
ACGGAGAGGA	CTGGATCTCC	CTGAAAGAGG	GAAATAAAGC	CATTATCTTT	CAGGGAAACA	1500	
CCAACCCAC	AGATGTTGTC	TTAGGAGTTT	TCTCCAAACC	ACTGATAACT	CGATTTGTTC	1560	
GAATCAAACC	TGTATCCTGG	GAAACTGGTA	TATCTATGAG	ATTGAAAGTT	TATGGCTGCA	1620	
AGATAACAGA	TTATCCTTGC	TCTGGAATGT	TGGGCATGGT	GTCTGGACTT	ATTTCAAGCT	1680	
CCCAGATTAC	AGCATCCAAT	CAAGCCGACA	GGAATTGGAT	GCCAGAAAAC	ATCCGTCTGG	1740	

FIG. 7-1



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1800 TGACCAGTCG TACCGGCTGG GCACTGCCAC CCTCACCCCA CCCATACACC AATGAATGGC  
1860 TCCAAGTGGA CCTGGGAGAT GAGAAGATAG TAAGAGGTGT CATCATTCAG GGTGGGAAGC  
1920 ACCGAGAAAA CAAGGTGTTT ATGAGGAAGT TCAAGATCGC CTATAGTAAC AATGGCTCTG  
1980 ACTGGAAAAAC TATCATGGAT GACAGCAAGC GCAAGGCTAA GTCGTTTCGAA GGCAACAACA  
2040 ACTATGACAC ACCTGAGCTT CGGACGTTT GCTCTCTCTC CACAAGGTTT ATCAGGATCT  
2100 ACCCTGAGAG AGCCACACAC AGTGGGCTTG GGCTGAGGAT GGAGCTACTG GGCTGTGAAG  
2340 CATACGGTTT TAACTGCCAG TTGGCTGGG GCTCTCACAA GACATTTCTGC CACTGGGAGC  
2400 ATGACAGCCA TGCACAGCTC AGGTGGAGTG TGCTGACCAG CAAGACAGGG CCGATTCAGG  
2460 ACCATACAGG AGATGGCAAC TTCTATCTATT CCCAAGCTGA TGAAAATCAG AAAGGCAAAAG  
2520 TAGCCCGCCT GGTGAGCCCT GTGGTCTATT CCCAGAGCTC TGCCCACTGT ATGACCTTCT  
2580 GGTATCACAT GTCCGGCTCT CATGTGGGTA CACTGAGGGT CAAACTACGC TACCAGAAGC  
2640 CAGAGGAATA TGATCAACTG GTCTGGATGG TGTTGGGCA CCAAGGAGAC CACTGGGAAG  
2700 AAGGACGTGT CTTGCTGCAC AAATCTCTGA AACTATATCA GGTATTTTT GAAGGTGAAA  
2760 TCGGAAAAAGG AAACCTTGGT GGAATTGCTG TGGATGATAT CAGTATTAAC AACCATATTT  
2820 CTCAGGAAGA CTGTGCAAAA CCAACAGACC TAGATAAAAA GAACACAGAA ATTAAAAATTG  
2880 ATGAACACAGG GAGCACTCCA GGATATGAAG GAGAAGGGGA AGGTGACAAG AACATCTCCA  
2940 GGAAGCCAGG CAATGTGCTT AAGACCCCTGG ATCCCATCTT GCTGTACTGT GCCTGTGTGGC  
3000 GTGCCCTGGG AGTACTCCTG GGTGCAGTCT GTGGAGTTGT GCTGTACTGT GCCTGTGTGGC  
3060 ACAATGGGAT GTCAGAAAGG AACCTATCTG CCTTGGAGAA CTATAACTTT GAACCTGTGG  
3120 ATGGTGTAAG GTTGAAAAAA GATAAACTGA ACCCACAGAG TAATTACTCA GAGGCGTGAA  
3180 GGCACGGAGC TGGAGGGAAC AAGGGAGGAG CACGGCAGGA GAACAGGTGG AGGCATGGGG  
3240 ACTCTGTTAC TCTGCTTTCA CTGTAAGCTG GGAAGGGCGG GGACTCTGTT ACTCCGCTTT  
3300 CACTGTAAGC TCGGAAGGC ATCCACGATG CCATGCCAGG CTTTTCTCAG GAGCTTCAAT  
3360 GAGCGTCACC TACAGACACA AGCAGGTGAC TGCGGTAACA ACAGGAATCA TGTACAAGCC  
3420 TGCTTTCTTC TCTTGGTTTC ATTTGGGTAA TCAGAAAGCCA TTGAGACCA AGTGTGACTG  
3480 ACTTCATGGT TCATCCTACT AGCCCCCTTT TTTCTCTCT TTTCTCCTTAC CCTGTGGTGG  
3540 ATTCTTCTCG GAAACTGCAA AATCCAAGAT GCTGGCACTA GCGGTTATTC AGTGGGCCCT  
3600 TTTGATGGAC ATGTGACCTG TAGCCCACTG CCCAGAGCAT ATTATCATAA CCACATTTCA  
3652 GGGGACGCCA ACGTCCATCC ACCTTTGCAT CGCTACCTGC AGCGAGCACA GG

FIG. 7-2